

Supplementary file 1. Pathogenic *PYGM* genotype indicative of McArdle disease identified in all the participants ($N = 54$)

Type of mutation	<i>N</i>
p.R50X (c.148C > T) / p.R50X (c.148C > T)	19
p.R50X (c.148C > T) / p.W798R (c.2392 T > C)	6
p.G205S (c.613G > A) / p.G205S (c.613G > A)	5
p.R50X (c.148C > T) / p.G205S (c.613G > A)	2
p.R50X (c.148C > T) / p.K754fsX49 (c.2262delA)	2
p.C784X (c.2352C > A) / p.R94W (c.280C > T)	1
p.R50X (c.148C > T) / p.R94W (c.280C > T)	1
p.R50X (c.148C > T) / p.R602W (c.1804C > T)	1

p.R50X (c.148C > T) / p.A660D (c.1979C > A)	1
p.R50X (c.148C > T) / p.E383K (c.1147G > A)	1
p.G205S (c.613G > A) / c.1768 + 1G > A	2
p.R50X (c.148C > T) / c.1768 + 1G > A	1
p.R50X (c.148C > T) / p.A365V (c.1094C > T)	1
p.R50X (c.148C > T) / p.A55GfsX21 (c.163_167delGCTCT)	1
p.R50X (c.148C > T) / p.A704V (c.2111C > T)	1
p.R50X (c.148C > T) / p.D534fsX5 (c.1601delA)	1

p.R50X (c.148C > T) / p.L5VfsX22 (c.13_14delCT)	2
p.R50X (c.148C > T) / p.R194W (c.580C > T)	2
p.R50X (c.148C > T) / p.R715W (c.2143C > T)	1
p.R50X (c.148C > T) / p.T488 N (c.1463C > A) + p.K215 K (c.645G > A)	2
p.R576X (c.1726C > T) / p.G136AfsX159 (c.407G > A)	1

Supplementary file 2. Physiological responses to the second wind and ramp tests in physically active female patients (n=7) vs their inactive referents (n=17).

Variable	12-minute constant load test for second wind detection*				Ramp test until exhaustion							
			Ventilatory threshold						Peak values			
	Active	Inactive	p-value between groups	ES (Hedge's g)	Active	Inactive	p-value between groups	ES (Hedge's g)	Active	Inactive	p-value between groups	ES (Hedge's g)
% of VO ₂ peak (ml·min ⁻¹)	64.4±19.2	66.9±11.7	0.707	0.17	69.2±13.5	64.4±13.5	0.468	0.34	-	-	-	-
VO ₂ (ml·kg ⁻¹ ·min ⁻¹)	12.2±2.2	10.9±3.4	0.420	0.40	13.5±3.4	10.1±2.2	0.012	1.27	20.1±5.8	16.4±4.8	0.147	0.70
Power output (watts)	31.6±12.5	24.1±5.6	0.056	0.89	47.5±25.1	27.1±8.4	0.007	1.31	86.3±30.9	65±9.4	0.017	1.14
HR (bpm)	149.6±15.5	144.1±20.1	0.547	0.28	125.8±15.5	113.1±15.5	0.102	0.79	170.5±13.7	152.5±16.7	0.029	1.09
V _E (l·min ⁻¹)	26.1±14.1	23.2±5.8	0.482	0.31	21±7.9	17.9±3.6	0.224	0.58	44.1±24.1	34.5±6.9	0.155	0.66
RER	0.84±0.08	0.83±0.10	0.871	0.10	0.82±0.08	0.8±0.12	0.718	0.17	0.93±0.07	0.87±0.13	0.314	0.49
% age-predicted HRmax	77.8±11.5	79.1±9.2	0.782	0.12	73.7±6.7	74.4±8.2	0.860	0.09	88.3±7.6	83.9±8.5	0.279	0.51

Abbreviations: HRmax, maximum heart rate (age predicted = 220 minus age in years); RER, respiratory exchange ratio; V_E, pulmonary ventilation; VO₂, oxygen uptake. VO_{2peak}, oxygen uptake. Symbol: * Average values for all variables correspond to the highest 10-second value of HR obtained during the constant-load test for second wind detection (which on average was reached at 6 min 35 s ± 94 s).

Supplementary file 3. Physiological responses to the second wind and ramp tests in physically active male patients (n=13) vs their inactive referents (n=17).

Variable	12-minute constant load test for second wind detection*				Ramp test until exhaustion							
			Ventilatory threshold						Peak values			
	Active	Inactive	p-value between groups	ES (Hedge's g)	Active	Inactive	p-value between groups	ES (Hedge's g)	Active	Inactive	p-value between groups	ES (Hedge's g)
% of VO ₂ peak (ml·min ⁻¹)	73.5±15.9	65.1±13.4	0.125	0.56	63.2±15.4	56.9±6.4	0.141	0.54	-	-	-	-
VO ₂ (ml·kg ⁻¹ ·min ⁻¹)	15.7±3.5	12.1±3.5	0.009	1.00	13.4±3.2	10.3±1.9	0.003	1.18	21.5±4.2	18.3±4.2	0.052	0.74
Power output (watts)	41.1±10.6	32.3±10.9	0.035	0.79	48±15.6	34.8±10.5	0.012	0.99	95.4±25.3	84.2±21.3	0.200	0.47
HR (bpm)	156.7±15.1	143.7±25.9	0.118	0.57	124.2±10	109.2±14.7	0.004	1.13	167.2±22.9	160.1±22.9	0.407	0.30
V _E (l·min ⁻¹)	28.9±6.6	26.3±9.5	0.402	0.30	21.9±6.5	21.1±5.3	0.710	0.13	45.9±18.5	45.6±11.1	0.958	0.01
RER	0.86±0.04	0.84±0.06	0.426	0.37	0.8±0.7	0.83±0.8	0.382	0.03	0.9±0.11	0.94±0.13	0.365	0.31
% age-predicted HRmax	83.2±10.5	76.3±11.9	0.109	0.59	75.6±12.4	68.8±9.2	0.098	0.61	88.7±13.8	85.1±9.6	0.411	0.30

Abbreviations: HRmax, maximum heart rate (age predicted = 220 minus age in years); RER, respiratory exchange ratio; V_E, pulmonary ventilation; VO₂, oxygen uptake; VO_{2peak}, peak oxygen uptake. * Average values for all variables correspond to the highest 10-second value of HR obtained during the constant-load test for second wind detection (which on average was reached at 6 min 35 s ± 94 s).